REMARKS

Claims 5-6, 13-21 and 25-25 are pending in the instant application. Claims 11-12 are canceled and claims 2-4, 7-10 and 22-24 are withdrawn.

In response to the Examiner's comments and to expedite prosecution, applicant has canceled claim 12 and amended claim 5 to recite the subject matter of claim 12.

Applicant has amended claims 5, 6, 13-21 and 25 to recite a kit rather than a composition. Support for this amendment is provided throughout the specification (see, e.g., page 19, lines 3-32).

Applicant has amended claims 20 and 25 to depend from claim 5, and not claim 12, which has been canceled.

Applicant has added claim 26, which recites a kit wherein the opioid is selected from morphine, codeine, dihydrocodeine, levomthadone, and tilidin. Support for this amendment is provided at page 22 of the specification.

None of these amendments adds new matter.

THE REJECTIONS

35 U.S.C. §112, First Paragraph - Claims 5-6

The Examiner has rejected claims 5-6 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner contends that the specification does not provide enablement for coadministering any corticosteroid receptor agonists and any addictive drugs. However, the Examiner admits that the specification is enabling for coadministering the receptor agonists recited in claim 20 and the particular addictive drugs disclosed in claims 13-19 and in the working examples recited on page 22. Applicant amends in part and traverses in part.

First, applicant has amended claim 5 to recite the specific addictive drugs recited in claims 13-19.

Second, applicant has amended claim 5 to recite that the agonist is selected from those specifically recited in claim 12. Applicant respectfully submits that the specification is not enabling for only those agonists recited in claim 20 --namely, dexamethasone and corticosterone. The specification is enabling for other corticosteroid receptor agonists and mineralo-corticosteroid receptor agonists (see, e.g., page 21).

Moreover, the mechanism of action of all the receptor agonists described in the specification is similar. All the agonists act by interacting with the corticosteroid or mineralo-corticosteroid receptor. Applicant respectfully submits that it would be unduly burdensome to require applicant to test each and every corticosteroid receptor agonist and mineralo-corticosteroid agonist.

Accordingly, for all the above reasons, applicant requests that the Examiner withdraw the enablement rejection.

35 U.S.C. §112, Second Paragraph - Claims 5-6, 12-13, 20-21, and 25

The Examiner has rejected claims 5-6, 12-13, 20-21, and 25 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner has rejected various claim terms. Applicant will address each term separately.

"Pharmacodynamic equivalent thereof"

The Examiner has rejected the term "pharmacodynamic equivalent thereof" stating that it is not clearly defined in the specification. Applicant traverses.

Applicant respectfully submits that the term "pharmacodynamic equivalent" is definite and is a term readily understood by one of ordinary skill in the art. For example, the pharmacology textbook Goodman & Gilman's The Pharmacological Basis of Therapeutics, Ninth Edition defines pharmacodynamics as "the study of the biochemical and physiological effects of drugs and their mechanisms of action" (copy attached as Exhibit A). As such, a pharmacodynamic equivalent is a compound which will exert an equivalent action via the same mechanism.

For example, opioids mediate their biological effect via the opioid receptors. Accordingly, the skilled worker would understand that a pharmacodynamic equivalent of an opioid refers to any compound which mediates its biological effect via opioid receptors. Similarly, each of the other addictive agents exerts its biological effect via a particular mechanism. The skilled worker would readily understand that pharmacodynamic equivalents thereof refers to compounds

which exert their action via the same mechanism as the claimed addictive agents.

Moreover, the skilled worker would understand pharmacodynamic equivalents of the specific corticosteroid or mineralo-corticosteroid receptor agonists recited in the claims refers to any compound that mediates its biological effect via corticosteroid or mineralo-corticosteroid receptors.

"High dose" and "Higher amount for the initial dosage"

The Examiner asserts that a "high dose" and "higher amount for the initial dosage" in claim 6 renders the claim indefinite because these terms are relative. Applicant traverses.

Applicant respectfully submits that the terms "high dose" and "higher amount for the initial dosage" are clearly defined in the specification. The specification at pages 20-22 clearly describes the dosage ranges for the addictive drugs and the corticosteroid receptor agonists. Accordingly, applicant requests that the Examiner withdraw this rejection.

"Or"

The Examiner has objected to the recitation of "or" in claim 5 as being improper Markush claim language.

Applicant has adopted the Examiner's suggestion and amended the claim to recite "and." Applicant requests that the rejection be withdrawn.

35 U.S.C. § 102(b) - Claims 5-6, 12-13, 20-21, and 25

The Examiner has rejected claims 5, 12-13, 20-21 and 25 under 35 U.S.C. § 102(b) as being anticipated by Peyman (WO 98/42275) ("Peyman"). The Examiner asserts that Peyman discloses a pharmaceutical composition comprising an opioid in combination with the instant preferred corticosteroid receptor agonist such as cortisol, cortisone, prednisolone and dexamethasone. Applicant traverses.

Applicant respectfully submits that Peyman does not anticipate the amended claims of the instant application. The amended claims recite a kit comprising a first receptacle comprising at least one agonist selected from a corticosteroid receptor agonist, or a mineralo-corticosteroid receptor agonist, wherein the

corticosteroid receptor agonist or mineralo-corticosteroid receptor agonist is selected from the group consisting of cortisol, cortisone, cortisone acetate, corticosterone, prednisolone, prednisone, prednylidene, methylprednisolone, triamcinolone, betamethasone, dexamethasone, paramethasone, fluorcortolone, deflazacort, cloprednol, fludrocortisone, a pharmacodynamic equivalent thereof, and a combination thereof; and a second receptacle comprising an addictive drug responsible for the addictive disease, wherein the addictive drug is selected from the group consisting of opioid, nicotine, cannabinoid, amphetamine, cocaine, Crack, MDMA (Ecstasy), a pharmacodynamic equivalent thereof; and at least one agonist selected from the group consisting of a corticosteroid receptor agonist and a mineralo-corticosteroid receptor agonist, wherein the corticosteroid receptor agonist or mineralo-corticosteroid receptor agonist is selected from the group consisting of cortisol, cortisone, cortisone acetate, corticosterone, prednisolone, prednisone, prednylidene, methylprednisolone, triamcinolone, betamethasone, dexamethasone, paramethasone, fluorcortolone, deflazacort, cloprednol, fludrocortisone,

a pharmacodynamic equivalent thereof, and a combination thereof. Peyman does not disclose a kit as recited in the amended claims.

Moreover, in the present invention, the sequence of administration of the addictive drug (opioid) and the corticosteroid receptor agonist is important. According to the present invention, the patient is first treated with the corticosteroid, followed by the combination of the corticosteroid and opioid, and optionally followed by the administration of the opioid alone. Peyman, by contrast, simply discloses the administration of an opioid in combination with a corticosteroid in no specific order. Peyman does not disclose that the sequence of administration of the addictive drug and the corticosteroid is of any importance. Accordingly, applicant requests that the Examiner withdraw the novelty rejection.

35 U.S.C. § 103(a) - Claims 5-6, 12-13, 20-21, and 25

The Examiner has rejected claims 5-6, 12-13, 20-21 and 25 under 35 U.S.C. § 103(a) as being unpatentable over Capasso et al. (XP-002100182 ("Caspasso I")and XP-002100187 (Caspasso II)) and Montgomery et al.

(XP-002100181) ("Montgomery"). The Examiner asserts that Capasso I and Capasso II disclose that a corticosteroid such as dexamethasone is capable of inhibiting opioid dependency and is useful in a pharmaceutical composition for treating opioid dependency, such as morphine, by administering an effective amount of dexamethasone before or after administering an effective amount of morphine. The Examiner further asserts that Montgomery discloses that a corticosteroid such as cortisol is capable of reducing the severity of morphine withdrawal by administering dexamethasone before or after administering morphine. The Examiner states that none of Capasso I, Capasso II or Montgomery discloses a single composition comprising the particular addictive drug in combination with the particular known corticosteroid receptor agonist. The Examiner further states that none of Capasso I, Capasso II or Montgomery expressly discloses the employment of prednisolone in the treatment of opioid dependency. The Examiner concludes that it would have been obvious to one ordinary skilled in the art to combine the addictive drug and a known corticosteroid receptor agonist into a single composition. Applicant traverses.

First, the amended claims of the instant application recite a kit comprising a first receptacle comprising at least one agonist selected from a corticosteroid receptor agonist, or a mineralo-corticosteroid receptor agonist, wherein the corticosteroid receptor agonist or mineralo-corticosteroid receptor agonist is selected from the group consisting of cortisol, cortisone, cortisone acetate, corticosterone, prednisolone, prednisone, prednylidene, methylprednisolone, triamcinolone, betamethasone, dexamethasone, paramethasone, fluorcortolone, deflazacort, cloprednol, fludrocortisone, a pharmacodynamic equivalent thereof, and a combination thereof; and a a second receptacle comprising an addictive drug responsible for the addictive disease, wherein the addictive drug is selected from the group consisting of opioid, nicotine, cannabinoid, amphetamine, cocaine, Crack, MDMA (Ecstasy), a pharmacodynamic equivalent thereof; and at least one agonist selected from the group consisting of a corticosteroid receptor agonist and a mineralo-corticosteroid receptor agonist, wherein the corticosteroid receptor agonist or mineralo-corticosteroid receptor agonist is selected from the

group consisting of cortisol, cortisone, cortisone acetate, corticosterone, prednisolone, prednisone, prednylidene, methylprednisolone, triamcinolone, betamethasone, dexamethasone, paramethasone, fluorcortolone, deflazacort, cloprednol, fludrocortisone, a pharmacodynamic equivalent thereof, and a combination thereof. Nothing in any of Capasso I, Capasso II or Montgomery teaches or suggests a kit as recited in the amended claims.

Moreover, the teachings of Capasso I, Capasso II and Montgomery differ substantially from the claims of the instant invention, in that these documents disclose the use of dexamethasone or cortisol for treating opioid physical dependency, in particular, withdrawal symptoms.

In contrast, the instant invention relates to the prophylaxis of relapse, i.e., the treatment of the psychological dependence. In each of Capasso I, Capasso II and Montgomery the corticosteroid was administered during the withdrawal process in order to alleviate the withdrawal symptoms. In the present invention, the treatment with corticosteroid receptor agonist followed by the combination of a corticosteroid receptor agonist and opiate is subsequent to the conclusion of the

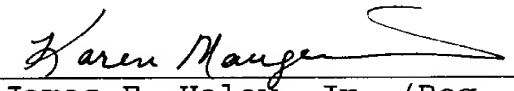
withdrawal period. Accordingly, for all the above reasons, applicant requests that the Examiner withdraw the obviousness rejection.

CONCLUSION

Applicant requests that the Examiner enter the amendments, consider the remarks herein, and allow the pending the claims.

The Examiner is invited to telephone applicant's representatives regarding any matter that may be handled by telephone to expedite allowance of the pending claims.

Respectfully submitted,



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APPENDIX

Exhibit A

GOODMAN & GILMAN'S The PHARMACOLOGICAL BASIS OF THERAPEUTICS

Ninth Edition

McGraw-Hill
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Goodman and Gilman's THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 9/e

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CHAPTER 2

PHARMACODYNAMICS

Mechanisms of Drug Action and the Relationship Between Drug Concentration and Effect

Elliott M. Ross

This chapter provides an introduction of the concept of receptors, the structural and functional families of receptors, and the interplay between the diverse signaling pathways activated by receptor occupancy. These introductory concepts are amplified in subsequent chapters detailing the structure and function of receptors for individual drug groups. The latter half of the chapter describes the historical development of receptor theory and presents means for quantifying receptor activation by agonists and blockade by antagonists. The functional relevance of partial agonists and inverse antagonists also is described as a prelude to the intentional development of mechanistically diverse drugs via classical or new combinatorial strategies.

Pharmacodynamics can be defined as the study of the biochemical and physiological effects of drugs and their mechanisms of action. The objectives of the analysis of drug action are to delineate the chemical or physical interactions between drug and target cell and to characterize the full sequence and scope of actions of each drug. Such a complete analysis provides the basis for both the rational therapeutic use of a drug and the design of new and superior therapeutic agents. Basic research in pharmacodynamics also provides fundamental insights into biochemical and physiological regulation.

MECHANISMS OF DRUG ACTION

The effects of most drugs result from their interaction with macromolecular components of the organism. These interactions alter the function of the pertinent component and thereby initiate the biochemical and physiological changes that are characteristic of the response to the drug. This concept—now obvious—had its origins in the experimental work of Ehrlich and Langley during the late nineteenth and early twentieth centuries. Ehrlich was struck by the high degree of chemical specificity for the antiparasitic and toxic effects of a variety of synthetic organic chemicals. Langley noted the ability of the South American arrow poison, curare, to inhibit the contraction of skeletal muscles caused by nicotine; however, the tissue remained responsive to direct electrical stimulation. The term *receptor* was coined to denote the component of the organism with which the chemical agent was presumed to interact.

The statement that the receptor for a drug can be any functional macromolecular component of the organism has several fundamental corollaries. One is that a drug potentially is capable of altering the rate at which any bodily function proceeds. Another is that drugs do not create effects, but instead modulate functions.

Drug Receptors

At least from a numerical standpoint, proteins form the most important class of drug receptors. Examples are the receptors for hormones, growth factors, and neurotransmitters, the enzymes of crucial metabolic or regulatory pathways (*e.g.*, dihydrofolate reductase, acetylcholinesterase), proteins involved in transport processes (*e.g.*, Na^+,K^+-ATPase), or proteins that serve structural roles (*e.g.*, tubulin). Specific binding properties of other cellular constituents also can be exploited. Thus, nucleic acids are important drug receptors, particularly for cancer chemotherapeutic agents.

A particularly important group of drug receptors are proteins that normally serve as receptors for endogenous regulatory ligands (*e.g.*, hormones, neurotransmitters). Many drugs act on such physiological receptors and are often particularly selective, because physiological receptors are specialized to recognize and respond to individual signal-